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### Authors

Campbell, Laura M
Paolillo, Emily W
Bryan, Robert
et al.



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# Informing Informed Consent for HIV Research

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**Laura M. Campbell[1], Emily W. Paolillo[1], Robert Bryan[2], Jennifer Marquie-Beck[2], David J. Moore[2], Camille Nebeker[3,4*], and Raeanne C. Moore[2*]**

**Abstract**

"Respect for Persons" is an ethical principle demonstrated through the informed consent process. Participants at a large HIV research center were surveyed to identify important aspects of the consent process. Persons with and without HIV ($n = 103$) completed a short pre/post questionnaire with both open-ended and forced choice response options. Qualitative analysis resulted in eleven themes about the most important consent elements which did not differ by HIV serostatus. Overall, participants rated the informed consent content and presentation by research staff as "extremely informative" and found the consent information to be "extremely consistent" with their study experience. Study results support the value of an interactive process and can be used to inform the design of a standardized, digital consent process.

**Keywords**

research ethics, HIV/AIDS, bioethics, research integrity, human subjects protection, vulnerable populations, mental health, clinical research

## Introduction

Obtaining informed consent for human participation in research is a regulatory obligation; however, it is also an ethical priority. Every effort should be made to ensure all aspects of study participation are clearly presented and easy to understand (Department of Health, Education, and Welfare, 2014; World Medical Association, 2013). Institutional review boards (IRB) are the administrative bodies that enforce the federal regulations for protection of human research subjects with a goal of evaluating the probability and magnitude of potential risks of harm against potential benefits of knowledge gained, recommending strategies for managing risks and generally promoting rigorous and ethical research. Although IRBs are responsible for reviewing and approving the information presented about a study, the actual process of obtaining informed consent from a potential research participant can vary both within and across studies. As a result, the informed consent delivery processes can range from simply letting the prospective participants review the informed consent information alone (e.g., electronic consent) to actively engaging with individuals in a face-to-face discussion (with or without visual/multimedia aids) to increase the likelihood that study information is understood by the prospective volunteer to make a decision about participation (Grady, 2015; Hallinan et al., 2016; Nishimura et al., 2013).

Whereas informed consent is a cornerstone of behavioral and biomedical research ethics (National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979), there are no requirements to assess whether the informed consent process used in a particular study is effective in facilitating authentic informed consent. Research on this topic, however, suggests as many as 50% of participants do not understand some or all components of informed consent across surgical and clinical trials (Appelbaum et al., 2004; Falagas et al., 2009; Tam et al., 2015). There are likely several reasons for this: (1) the inclusion of research-oriented language with which many participants may not be familiar (Bickmore et al., 2009); (2)

[1]San Diego State University/University of California San Diego Joint Doctoral Program in Clinical Psychology, San Diego, CA, USA
[2]Department of Psychiatry, University of California San Diego, La Jolla, CA, USA
[3]Department of Family Medicine and Public Health, School of Medicine, University of California San Diego, La Jolla, CA, USA
[4]Center for Wireless and Population Health Systems, Qualcomm Institute, University of California San Diego, La Jolla, CA, USA

*Joint Senior Authors

**Corresponding Author:**
Raeanne C. Moore, Department of Psychiatry, University of California San Diego, HIV Neurobehavioral Research Program, 220 Dickinson Street, Suite B (8231), San Diego, CA 92103, USA.
Email: r6moore@health.ucsd.edu

the inclusion of complex, IRB-required language addressing liability (Sieber & Levine, 2006); and (3) the extensive length of consent documents, which often makes them difficult to navigate and comprehend (Sieber & Levine, 2006). Individual IRBs typically require informed consent documents be at or below a certain grade reading level, often ranging from 5th grade to 10th grade reading levels (Paasche-Orlow et al., 2003); however, many informed consent documents have reading levels well above those standards (Paasche-Orlow et al., 2013). For example, one study examined readability of 124 HIV clinical trial consent forms and found median readability of 9.2 grade level, with confidentiality sections at a median of 12.6 grade level and overall document length almost 30 pages on average (Kass et al., 2011).

Ensuring participants are satisfied with the informed consent process is particularly important at research facilities that have long-term relationships with participants (e.g., where one may participate in several different ongoing studies over time), and/or among vulnerable patient populations that may have particularly strong concerns about privacy protections and data confidentiality. For example, HIV is an acquired and potentially transmissible disease that is stigmatized in both social and medical settings (Geter et al., 2018; Parker & Aggleton, 2003; Rueda et al., 2016). Although the body of research on people living with HIV (PWH) is vast, there is only one study that specifically evaluated the thoughts of PWH on the informed consent process (Tindall et al., 1994). This study, conducted 25 years ago, assessed the informed consent process for an HIV drug trial and found approximately 56% of participants reported understanding all information on informed consent forms and 21% thought too much information was included. Unfortunately, the authors did not evaluate participant thoughts about what information was the most or least helpful, which is necessary for improving the informed consent process. The lack of informed consent research among PWH highlights the need for greater understanding of how PWH perceive the informed consent process. This research on the consent process is essential if we are to improve the likelihood that consent is truly "informed," and, moreover, ensure individuals have the information needed to provide their voluntary agreement to participate in research. There are validated assessment tools used to evaluate informed consent comprehension (e.g., Jeste et al. (2007), Miller et al. (1996)). These tools have been useful particularly with populations with diminished cognitive capacity (Carpenter et al., 2000; Kim et al., 2001). While knowledge assessment tools can provide some indication that relevant information has been conveyed and, potentially understood, more research is needed to identify what influences meaningful and authentic informed consent.

The purpose of this study was to evaluate the informed consent process used at a large U.S. HIV research center among participants with and without HIV. An overarching goal was to better understand participant perceptions to inform improvements of the informed consent content and process. Specifically, we assessed aspects of the informed consent content that participants found most and least informative, and explored whether this differed by HIV serostatus. We also examined the efficacy of our informed consent process by assessing (after completing their study visit) whether participants thought the information presented was consistent with what they experienced during the study.

## Methods

### *Participants*

Participants ($n = 103$) enrolled in ongoing studies at the HIV Neurobehavioral Research Program (HNRP) completed a questionnaire regarding their experience with the informed consent process. The questionnaire was administered to participants immediately after enrolling as well as after completing their study visit. All participants were taken through the informed consent process on the same day as their study visit. All participants who came to the HNRP between May 5, 2017 and July 11, 2017 were invited to complete the consent questionnaire. One participant declined due to the paperwork burden of the primary study in which they were enrolled. The participants who chose to enroll in the present study were enrolled in a wide variety of both cross-sectional and longitudinal studies ranging in complexity and length of assessment that involved completion of self-report measures (e.g., evaluating domains such as mood, daily functioning), neuropsychological testing, and participation in clinical trials designed to test the efficacy of new drugs for improving cognition and physical outcomes among PWH.

### *Procedures and Measures*

A recruiter from the HNRP was responsible for presenting the informed consent information for this study to our existing HNRP participants. On average, recruitment staff have been with the HNRP for 9.8 years (range = 3.3–16) and have an established professional relationship with study participants.

Our recruitment staff adhere to a standardized informed consent process as follows. A recruiter sits across from the participant in a quiet screening room to ensure privacy during the consenting process. Typically, only one recruiter is present with one participant, unless particular expertise is needed from additional staff. In this case, and with the participant's permission, another recruiter may be brought in to assist and offer additional information. The consent process involves conveying study information to a prospective participation and usually requires approximately 30-minutes,

but the time can vary depending on the complexity of the study. During the informed consent process, the recruiter gives the prospective participant a copy of the "Experimental Subjects Bill of Rights" to review, which is required by California state law when enrolling in biomedical research that involves medical experimentation. The recruiter explains the HNRP's privacy practices and data confidentiality procedures, including that participants' identifying information (e.g., name, birthdate) is stored securely and separately from information collected for the study and only specific research staff have access to that information. Next, the recruiter reviews each paragraph of the IRB-approved study consent document with the prospective participant. At the end of each consent section, the recruiter asks if the prospective participant has any questions or concerns. Across studies hosted by the HNRP, the consent documents contain language required by the IRB, standard HNRP practices, and study specific information resulting in documents that range from 4 to 17 pages. Lastly, participant's knowledge of the study is tested with a validated assessment tool (i.e., UCSD Brief Assessment of Capacity to Consent, Jeste et al., 2007), which is used to evaluate understanding of the study purpose and procedures, including possible risks and benefits.

For this study, individuals who agreed to participate in a HNRP study following the consent process were asked to complete a written questionnaire with the following questions: (1) "What was the most important information that you learned during the informed consent presentation that helped you make a decision about participating" (open-ended response); (2) "What was the least important?" (open-ended response); (3) "How informative was the consent form?" (*1 = Not very informative* to *10 = Extremely informative*); and (4) "What did you think of the consent presentation?" (*1 = Not very informative* to *10 = Extremely informative*). Participants also completed one follow-up item at the end of their study visit: (5) "How consistent was the information presented during the consent process earlier today with what you actually did?" (*1 = Not Very Consistent* to *10 = Extremely Consistent*).

### Qualitative Coding

Two raters (LMC and ASR) independently coded participants' responses to questions 1, and 2, which were open-ended prompts where participants could write as much or as little as they wanted. Each rater established their own codebook organized by emerging patterns and themes. After initial coding of the responses, the raters and senior author (RCM) met to review the themes generated. The majority of codes and resulting themes were initially agreed-upon by both raters with discrepant themes discussed with the senior author until reaching inter-rater agreement. Theme labels were determined by group consensus.

### Statistical Analyses

Differences by HIV serostatus in response to qualitatively coded questions (i.e., questions 1, 2) on the consent questionnaire were assessed via Chi-Square test, and differences on questions using the 1–10 scale (i.e., questions 3–5) were assessed via Wilcoxon Rank Sums test. Correlations between number of visits previously completed at the research center and rating on questions 3–5 were assessed using Spearman's Rank Order Correlation. Analyses were conducted in JMP version 14.0.0.

## Results

One hundred and three participants completed the majority of the questionnaire. On average, participants were 54-years-old, 71% were male, 55% were Non-Hispanic White, and had 14.5 years of education. To further characterize the sample by HIV serostatus groups, HIV disease characteristics, cognitive status, and psychiatric and substance use characteristics of the participants are presented in Table 1.

### Most and Least Important Information Presented

Eighty-nine participants provided a legible written response to question one, which asked the most important information learned from the informed consent process. Fifteen participants' responses fell into more than one theme. Eleven themes emerged (Table 2), and the top five responses were: helping others/research (30.3%; e.g., "that it will help others in the future," "I would be helping people globally by participating in the study," and "that the study benefits medical research, AIDS/HIV"), confidentiality (23.6%; e.g., "that my information would be protected," "that my personal information will not be made public," and "what the information would be used for in regards to research"), information about the study procedures (18.0%; e.g., "the general procedure since it covered the events to be expected," "explanation of what was needed," and "what the study aims are"), information about subject rights (19.1%; e.g., "nothing happens to me unless I affirmatively agree to it," "that I could quit at any time if I felt uncomfortable," and "voluntary nature of my participation"), and helping self/personal interest (13.5%; "I would like to test my memory and see about my level of concentration—personal observation," "getting more information about my health and mind," and "the more I know about living with HIV the better"). Participant responses to the most important information in the informed consent presentation did not significantly differ by HIV serostatus ($p$'s $> .05$).

Sixty-six participants provided a response to question two, which asked what the least important information provided in the informed consent. Of the 66 participants who

**Table 1.** Demographics and Clinical Characteristics.

| | HIV+ ($n=63$) | HIV– ($n=40$) | Test-statistic[a] | $p$-value |
|---|---|---|---|---|
| *Demographics* | | | | |
| Age (years) | 55 (11.8) | 53 (15.8) | 0.57 | .57 |
| Sex (male) | 54 (86%) | 19 (48%) | 17.31 | <.01 |
| Race/Ethnicity | — | — | 4.62 | .20 |
| Non-Hispanic White | 30 (48%) | 27 (68%) | — | — |
| African American | 15 (24%) | 4 (10%) | — | — |
| Hispanic | 14 (22%) | 7 (18%) | — | — |
| Other | 4 (6%) | 2 (5%) | — | — |
| Education (years) | 13.8 (3.2) | 15.7 (2.3) | 3.30 | <.01 |
| Number of visits previously completed[c] | 9 [4.5, 19] | 1 [0, 7] | −4.36 | <.01 |
| *HIV characteristics* | | | | |
| AIDS Diagnosis[d] | 33 (63%) | — | — | — |
| Detectable viral load[b, e] | 5 (13%) | — | — | — |
| Current CD4 count[d] | 689 [460.5, 834.5] | — | — | — |
| Nadir CD4 count[f] | 199 [42.25, 350] | — | — | — |
| Estimated duration of infection[d] | 20.0 (9.2) | — | — | — |
| On antiretroviral therapy[d] | 43 (74%) | — | — | — |
| *Laboratory-based neurocognitive ability* | | | | |
| GDS-Impaired[g] | 19 (56%) | 5 (56%) | 0.01 | .99 |
| *Psychiatric and substance use characteristics* | | | | |
| Current psychiatric diagnosis[h] | 6 (16%) | 0 (0%) | 1.81 | .18 |
| LT psychiatric diagnosis[d] | 31 (74%) | 3 (30%) | 6.85 | <.01 |
| Current alcohol use disorder[h] | 1 (3%) | 0 (0%) | 0.27 | .60 |
| LT alcohol use disorder[d] | 18 (43%) | 4 (40%) | 0.03 | .87 |
| Current cannabis use disorder[h] | 3 (8%) | 0 (0%) | 0.84 | .36 |
| LT cannabis use disorder[d] | 12 (29%) | 2 (20%) | 0.30 | .58 |
| Current methamphetamine use disorder[h] | 0 (0%) | 0 (0%) | — | — |
| LT methamphetamine use disorder[d] | 12 (29%) | 2 (20%) | 0.30 | .58 |
| *Consent questionnaire* | | | | |
| Question 3: how informative | 9.3 (1.3) | 9.3 (1.1) | 0.02 | .99 |
| Question 4: rating of presentation | 9.3 (1.3) | 9.4 (1.0) | 0.31 | .75 |
| Question 5: consistency | 9.0 (1.7) | 9.6 (0.7) | 1.14 | .25 |

*Note.* Values are presented as mean (SD), median [IQR], or N (%).
GDS = Global Deficit Score, an algorithmic approach to classifying neurocognitive impairment (Carey et al., 2004); LT = Lifetime.
[a]T-tests or Wilcoxon Rank Sums for continuous variables; $Chi^2$ for dichotomous variables.
[b]Plasma; Defined as >50 copies/mL.
[c]($n=85$); [d]($n=52$); [e]($n=38$); [f]($n=55$); [g]($n=43$); [h]($n=48$).

provided a response, 38 (57.6%) indicated everything was important (e.g., "everything is important," and "none"; PWH $n=27$, 64.3%; HIV– $n=11$, 47.8%). Information about compensation was endorsed as least important by 10.6% of respondents (e.g., "the compensation," "being paid to participate"; PWH $n=4$, 9.3%, HIV– $n=3$, 13.0%). There were no other consistent responses among participants that were endorsed by more than 8% of the sample.

## *Informativeness and Consistency of Information Presented*

Overall, participants found the consent content and the delivery process to be extremely informative (Question 3: $n=99$, M=9.3, SD=1.2; Question 4: $n=100$, M=9.3, SD=1.2). These scales ranged from *1 = not very informative* to *10 = extremely informative*, and participant scores ranged from 5 to 10. Eighty-four participants received the second part of the questionnaire after their participation. Participants found the information presented during the consent process to be extremely consistent with what they actually did during the study (M=9.3, SD=1.4). The scale ranged from *1 = not very consistent* to *10 = extremely consistent*, and participant scores ranged from 5 to 10. There were no HIV serostatus differences in regard to participants' perceptions of informativeness or consistency of information presented ($p$'s > .05). Additionally, number of study visits completed at the research center was not correlated with informativeness or consistency ($p > .05$).

**Table 2.** "What Was the Most Important Information That You Learned During the Informed Consent Presentation That Helped You Make a Decision About Participating.".

| | HIV+ ($n = 52$) | HIV– ($n = 37$) |
|---|---|---|
| Helping others/research | 12 (23.1%) | 15 (40.5%) |
| Confidentiality | 10 (19.2%) | 11 (29.7%) |
| Information about the study procedures and time commitment | 10 (19.2%) | 6 (16.2%) |
| Information about subject rights/participation is voluntary | 9 (17.3%) | 6 (16.2%) |
| Helping self/personal interest | 9 (17.3%) | 3 (8.1%) |
| "Everything" | 3 (5.8%) | 0 (0%) |
| Nice sentiment about staff | 2 (3.8%) | 2 (5.4%) |
| Compensation | 2 (3.8%) | 1 (2.7%) |
| Ability to ask questions | 2 (3.8%) | 0 (0%) |
| Opportunities to participant in other studies | 1 (1.9%) | 0 (0%) |
| Information about risks/safety | 0 (0%) | 4 (10.8%) |

*Note*: Some participants did not provide a written response or response was illegible; Participants sometimes stated >1 response; all responses are included in Table.

## Discussion

In research studies, it is the responsibility of the researcher to ensure that the consent process is implemented correctly. While decisional capacity questionnaires are common, particularly in populations with higher risk of impaired decisional capacity, it is not common practice to solicit feedback from participants with regard to the informed consent process. Research participants at the HNRP, a research center with multiple years of working with PWH and dedicated research staff with experience taking potential research participants through the consent process, found the consenting process, on average, to be extremely informative and extremely consistent with what they did during the study. This indicates that the traditional informed consent process involving a face-to-face discussion with a prospective research participant combined with a written consent document can be successful. Additionally, several different themes were endorsed as "most important" and the most common answer for what was "least important" was that everything was important. This would indicate that although some participants do not find all portions of informed consent to be useful, some participants do; including the goals of the study, procedure, risks, and information about protection of confidentiality. This may also suggest the consenting process should be tailored (e.g., "MyTerms"; see Nebeker et al., 2019) to individual participants, and participants should be able to choose how much additional information they are provided beyond the required information.

We did not observe differences in response to any of the questions by HIV status. Unfortunately, there is little research examining what PWH value most from research study participation, the informed consent process in general, or in comparison to HIV-negative persons to compare with our findings. One review examining barriers to participation in HIV drug trials found societal discrimination and distrust of researchers, among other things (e.g., side-effects, pragmatic obstacles), were barriers to participation (Mills et al., 2006). Based on this review, as well as historical and ongoing stigma toward PWH, confidentiality may be something PWH highly value in research studies. However, in this study, we did not observe HIV serostatus differences in proportion of participants reporting confidentiality to be "most important." The majority of PWH participants who filled out the consent questionnaire have been in multiple studies at the center and, on average, have completed more study visits than HIV-negative participants. The center is also actively involved within the community. Therefore, participants prior experience with the center may have had a higher level of trust going into the informed consent process, which may have influenced their responses. Additionally, confidentiality is likely valued by many individuals regardless of HIV status, which also may be why we did not observe any difference by HIV serostatus.

While this study adds valuable insights into informed consent literature, there are limitations. First, the center in which this study took place is an established community research facility with highly trained staff experienced both working with this study population and consenting participants. Studies without these resources, trained staff, or established study enrollment practices may have difficulty with establishing the practices described in this study. Second, participants in the study were already willing to come in for the research study, so their responses may not accurately reflect what the general population values from the informed consent process or what aspects of the informed consent process may persuade individuals that are not willing to participate in research. Moreover, we were unable to examine responses by

other variables of interest (e.g., which study the participant enrolled; cognitive impairment; psychiatric and substance use disorders) due to sample size restrictions. Future studies should aim to assess participants' preferences with respect to information presented during the informed consent process and how those preferences differ at the individual level. Lastly, not all participants provided responses to every question, particularly the open-ended response questions, which may be due to participants not having feedback to provide (e.g., no additional comments) or found the open-ended response questions to be burdensome. Asking a more specific question or interviewing participants about what changes they would suggest for improving the informed consent process may have elicited more responses.

## Best Practices

This study demonstrates that implementing the informed consent process with trained staff can be successful. Participants reported the experience as both informative and believed what they were told during the consent process was consistent with what they experienced during the study. This is in line with systematic reviews that have found that the most effective way to improve understanding of the informed consent was to have a one-on-one discussion with study participants (Flory & Emanuel, 2004; Nishimura et al., 2013). This would suggest that IRBs and researchers should be invested in the training of those who implement the informed consent process as well as monitor how the informed consent is presented to research participants. Furthermore, our recommendation to researchers working with PWH is to view the informed consent process as an opportunity to build trust, educate and show a true appreciation for the participants' time, which will hopefully encourage continued participation in research.

## Research Agenda

There are opportunities to continue to improve the informed consent process, and there have been recent updates to the "Common Rule", which will influence the presentation of the informed consent moving forward (Hodge & Gostin, 2017). Often in practice the informed consent falls short of what it aims to accomplish (Grady, 2015). For example, a recent meta-analysis found that participants' understanding of portions of the informed consent ranged from 52–76% (Tam et al., 2015). Even more discouraging is that Tam et al. (2015) found that the proportion of participants who understood the informed consent process has not improved in the past 30 years. In hopes of improving informed consent to make it more engaging and understandable, two studies compared a simplified and concise informed consent with a traditional consent form. Both studies reported that participants found the shorter informed consent more engaging, and one study reported that comprehension was equivalent to the standard consent form whereas the other study found improved understanding with the shorter consent form (Garrett et al., 2017; Krishnamurti & Argo, 2016). Another study found that implementing a fact sheet and engaging in a question and answer feedback session improved open-ended questions to assess understanding of the informed consent (Kass et al., 2015). Additionally, in a study that compared ways to assess understanding of the informed consent, found that commonly-used forced choice or self-report questionnaires may overestimate the level of understanding of the informed consent as recognition of information does not ensure comprehension of information (Lindegger et al., 2006). Therefore, free-response questions may be a better measure of comprehension indicating that IRBs that review decisional capacity questionnaires and researchers who are trying to improve the informed consent process must be mindful of how understanding of the informed consent is assessed.

As research moves more toward digital studies and trials where the in-person interaction is not feasible, as we are currently facing with the COVID-19 crisis, it will be important to design the consent process that can build upon elements of existing successful consent models. Standards of practice and design features for digital consent, also known as eConsent, are in development. Some groups (e.g., Sage Bionetworks) have begun to create open-source and customizable tools for low-risk, mobile-mediated research (Doerr et al., 2016; Moore et al., 2017; Wilbanks, 2018), which has been used in patient populations (e.g., Parkinson's Disease; Doerr et al., 2017). Digital studies and eConsents are advantageous as they allow for use of multimedia methods (e.g., video, PowerPoint), which can be standardized and reviewed by an IRB to ensure that participants are receiving the necessary information. Studies that have examined multimedia methods have shown that they successfully relay information to participants, with some studies reporting that use of video or PowerPoint is related to an increase in engagement and comprehension (Hall et al., 2017; Palmer et al., 2012; Simon et al., 2018). Additionally, as more participants want their study results returned to them, digital consent could allow participants to tailor the consent to their personal preferences and select which data (if any) they would like access to (e.g., "MyTerms" as described in Nebeker et al. (2019)). However, there are additional considerations when designing eConsent (Wilbanks, 2018). For example, in a focus group study of patients underrepresented in research, participants overall found eConsent easy to use and interesting; however, minority and rural participants raised concerns about accessibility, trust, and confidentiality (Simon et al., 2018). We anticipate our findings demonstrating an engaging informed consent process can be adapted for digital deployment for populations that value privacy and confidentiality such as PWH.

## Educational Implications

Funders who support human research should support educational research with a goal of obtaining evidence to

inform best practices for obtaining authentic and meaningful informed consent to participate in research. Moreover, IRBs that oversee participant protections should support communication trainings to educate researchers on how to effectively convey informed consent information to research participants. Additionally, as digital consent approaches become more prevalent, IRBs should also provide guidance and training on what the research shows is the most effective way to communicate informed consent information on a digital platform. To successfully do this, we recommend IRBs engage with scientists and a diverse public in the process of developing training programs to ensure information quality, access and equity. Clearly, more research is needed to improve the informed consent process as well as inform best practices for the presentation of both in-person and digital informed consent.

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## ORCID iDs

Laura M. Campbell https://orcid.org/0000-0001-9790-1603
Raeanne C. Moore https://orcid.org/0000-0002-7499-041X

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## Author Biographies

**Laura M. Campbell** is a graduate student in the SDSU/UC San Diego Joint Doctoral Program in Clinical Psychology. Her research focuses on biological correlates of cognitive functioning and the use of digital technology to examine cognitive functioning in older adults and adults living with HIV. She led manuscript preparation and led qualitative scoring.

**Emily W. Paolillo** is a graduate student in the SDSU/UC San Diego Joint Doctoral Program in Clinical Psychology. Her research focuses on the use of digital technology to examine cognitive functioning in adults living with HIV and substance use. She contributed to manuscript writing and editing.

**Robert Bryan** is a Community Education Specialist at UCSD's HIV Neurobehavioral Research Program (HNRP). He led data collection and contributed to manuscript.

**Jennifer Marquie-Beck** is the director of Research Operations at UCSD's HNRP. She contributed to implementation of the project within the HNRP; contributed to manuscript; and provided edits.

**David J. Moore** is a professor of Psychiatry at UCSD and an investigator at the HNRP. Dr. Moore has an over 20-year history working with persons living with HIV at the HNRP. He contributed to implementation of the project within the larger HNRP context; contributed to manuscript; and provided edits to manuscript and analyses.

**Camille Nebeker** is an associate professor of Behavioral Medicine in the Department of Family Medicine and Public Health at UC San Diego. Her research focuses on research literacy capacity building and the ethical and social implications of technologies used in mobile health research. She contributed to the study conception, including survey development, and contributed to manuscript writing and editing.

**Raeanne C. Moore** is an associate professor of Psychiatry at UCSD and an investigator at the HNRP. Her research incorporates digital health technologies to improve the assessment of brain health in clinical research. Her role in this work included: conceived of the study; oversaw data collection; resolved discrepancies in inter-rater reliability; contributed to manuscript writing and editing.